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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,517	12/06/1999	BRADFORD J DUFT	235/013US	1018

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Intellectual Property Department
Amylin Pharmaceuticals, Inc.
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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/445,517	DUFT ET AL.	
	Examiner	Art Unit	
	S. DEVI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23, 25, 27-29, 31-33, 35, 37-39, 69-71, 73-80, 82, 84-90 and 95-97* is/are pending in the application.

4a) Of the above claim(s) *25, 28, 35, 69-71, 73-75, 77-79 and 85-90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,27,29,31-33,37-39,76,80,82,84 and 95-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendments

1) Acknowledgment is made of Applicants' amendments filed 01/04/11 and 11/30/10 in response to the non-final Office Action mailed 08/31/10.

Status of Claims

2) Claims 24, 26, 30, 34, 36, 68, 72 and 91-94 have been canceled via the amendment filed 01/04/11.

Claims 23, 25, 33, 35, 80 and 84-90 have been amended via the amendment filed 01/04/11.

Claims 23, 25, 27-29, 31-33, 35, 37-39, 69-71, 73-80, 82, 84-90 and 95-97 are pending.

Claims 23, 27-29, 31-33, 37-39, 76, 80, 82, 84 and 95-97 are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Moot

5) The rejection of claims 68 and 72 made in paragraph 35 of the Office Action mailed 05/30/06 and maintained in in paragraph 33 of the Office Action mailed

08/31/10 under 35 U.S.C § 112, first paragraph, as being non-enabled with regard to the scope, is moot in light of Applicants' cancellation of the claims.

6) The rejection of claims 24 and 34 made in paragraph 34 of the Office Action mailed 05/30/06 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 35 of the US patent 5,686,411 issued to Gaeta et al. ('411, of record) as evidenced by Tsanev (Vutr. Boles 23: 12-17, 1984, abstract, of record), is moot in light of Applicants' cancellation of the claims.

Rejection(s) Withdrawn

7) The provisional rejection of the instant claims made in paragraph 26 of the Office Action mailed 05/30/06 and maintained in paragraph 31 of the Office Action mailed 08/31/10 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of the co-pending application, SN 08/870,762, is withdrawn in light of the issuance of the co-pending application and Applicants' amendments.

8) The provisional rejection of claims 33 and 82 made in paragraph 28 of the Office Action mailed 05/30/06 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 6 of the co-pending application, 10/851,574, and maintained in paragraph 31 of the Office Action mailed 08/31/10, is withdrawn in light of the issuance of the co-pending application and Applicants' amendments.

9) The rejection of claims 76, 84 and 97 made in paragraph 35 of the Office Action mailed 05/30/06 and made or maintained in in paragraph 33 of the Office Action mailed 08/31/10 under 35 U.S.C § 112, first paragraph, as being non-

enabled with regard to the scope, is maintained for reasons set forth therein and herein below.

10) The rejection of claims 23 and 33 made in paragraph 34 of the Office Action mailed 05/30/06 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 35 of the US patent 5,686,411 issued to Gaeta et al. ('411, of record) as evidenced by Tsanev (Vutr. Boles 23: 12-17, 1984, abstract, of record), is withdrawnin light of Applicants' amendments to the claims.

Double Patenting Rejection(s)

11) Claim 76 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4, 6 and 7 of US patent 7,910,548. Although the conflicting claims are not identical, they are not patentably distinct from each other. The method of treatment claimed in the above-identified claims of the '548 patent is for the treatment of obesity in a human in need thereof wherein pramlintide (^{25,28,29}Pro-human amylin) is administered as recited. The method claimed therein anticipates the instantly claimed treatment method.

12) Claims 23 and 33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 31 of the US patent 5,686,411 issued to Gaeta et al. (of record) as evidenced by Tsanev (Vutr. Boles 23: 12-17, 1984, abstract, of record).

Although the conflicting claims are not identical, they are not patentably distinct from each other. The method claimed in claim 31 of the US patent 5,686,411 is for the treatment of diabetes mellitus in a mammal comprising the administration to said mammal of a therapeutically effective amount of the amylin

agonist analogue of claim 6, i.e., an amylin agonist analogue of instantly recited SEQ ID NO: 14. The portion of the disclosure of the '411 patent at lines 45-53 in column 7 that supports the limitation mammal does not exclude, but expressly includes a patient seen by a medical practitioner, i.e., a human. The portion of the disclosure of the '411 patent at lines 53-59 in column 8 supporting the limitation 'therapeutically effective amount' of the amylin agonist includes the dosage units of 0.1 to 5 mg of the agonist. The portion of the disclosure of the U.S. patent '411 at lines 9-12 of column 3 that describes the limitation 'diabetes mellitus' includes insulin-requiring diabetes mellitus. Given the art-known fact that upto 90% of diabetic patients are intrinsically obese as disclosed by Tsanev, the method of the '411 patent comprising the step of administration of a therapeutically effective amount of the amylin agonist analogue of claim 6 to a diabetic human anticipates the instant claims. Given that the method step of the '411 patent and the instant claims is the same, the method of the '411 patent is expected to bring about a therapeutic effect against the intrinsic obesity in the diabetic patients as defined in the instant invention, i.e., by controlling weight for cosmetic purposes, or to improve bodily appearance in the diabetic patients.

13) Claim 76 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 35 of the US patent 5,686,411 issued to Gaeta et al. (of record) as evidenced by Tsanev (Vutr. Boles 23: 12-17, 1984, abstract, of record).

Although the conflicting claims are not identical, they are not patentably distinct from each other. The method claimed in claims 34 and 35 of the US patent 5,686,411 is for the treatment of diabetes mellitus in a mammal comprising the administration to said mammal of a therapeutically effective amount of the amylin

agonist analogue of claim 19, i.e., ^{25,28,29}Pro-human amylin. The portion of the disclosure of the '411 patent at lines 45-53 in column 7 that supports the limitation mammal does not exclude, but expressly includes a patient seen by a medical practitioner, i.e., a human. The portion of the disclosure of the '411 patent at lines 53-59 in column 8 supporting the limitation 'therapeutically effective amount' of the amylin agonist includes the dosage units of 0.1 to 5 mg of the agonist. The portion of the disclosure of the U.S. patent '411 at lines 9-12 of column 3 that describes the limitation 'diabetes mellitus' includes insulin-requiring diabetes mellitus. Given the art-known fact that upto 90% of diabetic patients are intrinsically obese as disclosed by Tsanev, the method of the '411 patent comprising the step of administration of a therapeutically effective amount of the amylin agonist ^{25,28,29}Pro-human amylin to a diabetic human anticipates the instant claims. Given that the method step of the '411 patent and the instant claims is the same, the method of the '411 patent is expected to bring about a therapeutic effect against the intrinsic obesity in the diabetic patients as defined in the instant invention, i.e., by controlling weight for cosmetic purposes, or to improve bodily appearance in the diabetic patients.

Rejection(s) under 35 U.S.C. § 112, First Paragraph

14) The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15) Claims 23, 27, 29, 31-33, 37-39, 76, 80, 82, 84 and 95-97 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Instant claims are evaluated based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

As amended, the claimed method is of treating obesity in any human subject comprising or consisting of administering to said subject a composition comprising any peptide or any amylin agonist analogue comprising the amino acid sequence of SEQ ID NO: 14 as recited, wherein A1 is Lys, Ala, Ser, or hydrogen; B1 is Ala, Ser or Thr; C1 is Val, Leu or Ile; D1 is His or Arg; E1 is Ser or Thr; F1 is Ser, Thr, Gln, or Asn; G1 is Asn, Gln or His; H1 is Phe, Leu or Tyr; I1 is Ile, Val, Ala or Leu; J1 is Ser, Pro or Thr; K1 is Asn, Asp or Gln; X and Y are independently selected residues having side chains which are chemically bonded to each other to form an intramolecular linkage, wherein said intramolecular linkage comprises a disulfide bond, a lactam or a thioether linkage; and Z is an amino, alylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy; and provided that when A1 is Lys, B1 is Ala, C1 is Val, D1 is Arg, E1 is Ser, F1 is Ser, G1 is Asn, H1 is Leu, I1 is Val, J1 is Pro, and K1 is Asn; then one or more A to K1 is a D-amino acid and Z is selected from the group consisting of alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy,

aryloxy or aralkyloxy, or such a composition. In the method claimed in claim 76, the peptide is not administered in conjunction with another obesity relief agent. Claim 76, 84 and 97 encompass the administration of pramlintide species or SEQ ID NO: 14 in a method of treating obesity in a human in need thereof.

The genus 'human subject in need thereof' encompasses within its scope diabetic and non-diabetic humans, morbidly and non-morbidly obese humans etc. The amylin agonist analogue or the peptide of the recited structure of SEQ ID NO: 14 encompasses a large number of amylin agonist analogue or peptide variant subsequence species. A representative number of the species, if not each of the species, encompassed within the scope of the instantly claimed method is required to be effective in treating obesity in a diabetic or non-diabetic obese human subject, or a morbidly or non-morbidly obese human subject when administered not in conjunction with another obesity relief agent in the recited dose range. However, neither the art at the time of the invention, nor the instant specification demonstrates the obesity-treating function(s) of these peptide variant or amylin agonist analogue species in a diabetic or non-diabetic human in need of treatment of obesity upon administration via any route for any length of time. Whether or not the non-pramlintide species of amylin agonist analogues, which fall within the genus of SEQ ID NO: 14, are known in the art or mentioned in the instant specification, and whether or not the conventional assays for identifying amylin agonist analogues and for detecting amylin activity, are known in the art or described in the specification, is not the issue. Whether or not the non-pramlintide amylin agonist analogues mentioned in the specification or known in the art have been shown to mimic 'an effect' of amylin in vitro or in vivo, is not the issue. Given the breadth of the genus 'SEQ ID NO: 14', it is not possible to envisage

what precise structure in the genus of 'SEQ ID NO: 14' provides for the required functionality, i.e., the ability to treat obesity in a generic human subject in need thereof. The specification does not provide adequate guidance with regard to this. With regard to the amylin agonist analogue or peptide variant species, a review of the instant specification indicates that the showing in the instant specification is limited to the pramlintide species. With regard to the base claim 76, only pramlintide species at specific doses and via specific routes is shown to reduce body weight of a specific human population in need of treatment. However, outside this scope, neither the specification nor the art at the time shows that the amylin agonist analogues or peptide variants having a structure considerably different from that of pramlintide and falling within the scope of the SEQ ID NO: 14 genus, do retain the obesity-relieving biologic function(s). In other words, the instant specification fails to demonstrate that the peptide variant species or the amylin agonist analogue species having the recited amino acid substitutions or chemical modifications, if administered by one of skill in the art to a diabetic or non-diabetic obese human subject, or a morbidly obese human subject with or without diabetes, by subcutaneous or non-subcutaneous route in the amount range recited, would elicit a therapeutic effect against obesity. Precisely what structure of the amylin agonist analogue or the peptide variant 'SEQ ID NO: 14' genus provides for the recited functionality, i.e., ability to treat obesity in the broad genus of 'human subject in need thereof' is not identified. There is lack of enablement of non-pramlintide amylin agonist analogue or peptide variant species within the SEQ ID NO: 14 genus, each having the required functional ability to treat obesity in any human subject species in need thereof. It should be noted that predictability or unpredictability is one of the Wands factors for enablement. In the instant

application, Applicants have previously acknowledged that obesity is a complex, multifacorial disease that has been the subject of decades of research. Applicants have acknowledged that there are contradictions and confusion in the relevant art. See pages 22 and 23 of Applicants' response filed 09/02/04. Although Example 9 of the instant specification describes the gastric emptying assay and the effect of specific amounts of 'amylin' (as opposed to the amylin agonist analogue SEQ ID NO: 14) on gastric emptying in diabetic rats, and Examples 7 and 8 describe the receptor binding and soleus assays of some amylin variants, of the various biologic activities or functions attributed to amylin or pramlintide, which precise activity or activities provide for, or are associated with obesity relief in the 'human subject' genus has not been precisely identified. Of the various screenable activities, whether one activity, all the activities, or a specific combination of activities, are responsible for the obesity-relief function(s) was neither known in the art, nor is it established within the instant specification, absent which, one of skill in the art cannot practice the claimed invention without engaging in a considerable amount of undue experimentation. A mere screening of art-known amylin agonist analogue species falling within the genus of SEQ ID NO: 14 using the conventional screening assays does not enable one to reproducibly practice the claimed method of treatment. Whether or not the various amylin agonist analogue or peptide variant species encompassed within the scope of the SEQ ID NO: 14 genus have the required obesity relief function(s) was neither known nor could it be predicted. This is critically important in view of the Wands factor, predictability or unpredictability in the art. Applicants have previously stated that neither the amylin art nor the obesity art suggested or indicated an approach to trying an amylin or an amylin agonist (let alone an amylin agonist analogue) for

weight reduction or treatment of obesity. See bottom of page 57 of Applicants' response filed 09/02/04. With regard to what was known in the art at the time of the invention or thereafter, Applicants stated that Frishman et al. (In: Cardiovascular Pharmacotherapeutics. (Eds) Frishman WH et al. McGraw-Hill Health Professions Division, New York, Chapter 48, pages 1093-1114, February 1997, of record) 'only' concluded that 'the potential role of amylin in weight reduction 'awaits clinical investigation'. See the full paragraph on page 85 of Applicants' response filed 09/02/04. Applicants have recognized the importance of the unpredictability previously. For example, with regard to the gastric emptying function/activity and obesity, Applicants have previously taken the position that there is no agreement on the effect of gastric emptying in obesity. Applicants pointed to various reportings and stated that the role of gastric emptying in obesity was uncertain and controversial at the time of filing of the instant application, as well as before and after. See page 37 of Applicants' response filed 09/02/04. Applicants mentioned of the Minnesota Medical Association's recent reporting that gastric emptying is useful in treating diabetics, but researchers are 'uncertain' whether it will produce weight loss. See page 37 of Applicants' response filed 09/02/04. Applicants have gone on the record previously stating that any and all compounds having any gastric emptying activity are not necessarily useful for treating obesity, let alone one that is being evaluated for use in the treatment of diabetes. See lines 4-6 on page 85 of Applicants' response filed 09/02/04. With the art-known fact that obesity is a complex and multifactorial disease and with the precise amylin or pramlintide activity contributing to obesity relief being unknown at the time of the invention, there is no predictability that the recited peptide variants or amylin agonist analogues

having the recited amino acid substitutions or chemical modifications and being encompassed within the genus of SEQ ID NO: 14 would be therapeutically functional as effective obesity-relief agents in a human subject. Furthermore, the effects the various amino acid substitutions and/or chemical modifications would have on the activity of amylin agonist analogues or peptides which contribute to the reported undesired side effects, including recurrent nausea and vomiting and excessive anorexia, and the undesired properties such as insolubility and tendency toward aggregation, are also unpredictable. The various amino acid substitutions and/or chemical modifications encompassed within SEQ ID NO: 14 can potentially render the amylin agonist analogue species or peptide variant species more insoluble than amylin and unacceptably nausea- or vomiting-inducing. In sum, the instant specification simply lacks a concrete in vivo showing that a representative number of amylin agonist analogue or peptide species encompassed within the SEQ ID NO: 14 genus has obesity-relieving function in any human subject in need of the claimed method of treatment. Most importantly, at the time of the invention, amyin agonist analogues having amylin activities served as therapeutic agents for treating anorexia in a patient deficient in adipose tissue. See page 7 and 16 and claims 1 and 8 of Rink et al. (WO 92/20367, of record). The therapeutically effective amount of amylin for the treatment of anorexia was about 0.1 to 10 mg. See page 13. Note that the amount of SEQ ID NO: 14 recited in instant claims 23, 33, 80, 82 and 84 falls within this range. Rink et al. also discovered that two weeks of amylin administration resulted in no weight reduction in both dogs and rats. See page 11. With this knowledge in the art, there is no predictability that the amylin agonist analogue species encompassed within the genus SEQ ID NO: 14 would serve as anti-obesity therapeutic agents as opposed to anorexia-treating

agents. Due to the lack of specific guidance and direction, the lack of evidence and working examples enabling the full scope, the breadth of the claims, the quantity of experimentation necessary, and the art-recognized unpredictability, a considerable amount of undue experimentation would have been required to practice the instant invention. Instant claims clearly do not meet the enablement provision of 35 U.S.C. § 112, first paragraph.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

16) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

17) Claims 23, 27, 29, 31-33, 37-39, 80, 82, 95 and 96 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 23 is vague and indefinite because it has improper antecedent basis in the limitation: 'the amylin or amylin agonist'. See lines 3 and 4. There is no earlier recitation of an amylin or an amylin agonist.

(b) Claim 33 is vague and indefinite in the limitation: 'said amylin or amylin agonist'. See lines 4 and 5. There is no earlier recitation of an amylin or an amylin agonist.

(c) Analogous rejection and criticism apply to claims 80 and 82 with regard to the limitation 'the' or 'said' 'amylin or amylin agonist'.

(d) Claims 27, 29, 31, 32, 37-39, 80, 82, 95 and 96, which depend from claim 23 or 33, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C § 102

18) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> **(e)** the invention was described in-
> **(2)** a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

19) Claims 76, 84 and 97 are rejected under 35 U.S.C § 102(b) as being anticipated by Kolterman et al. (Diabetologia 39: 492-499, April, 1996, of record) (Kolterman et al., 1996) as evidenced by Itasaka et al. (Psychiatr. Clin. Neurosci. 54: 340-341, June 2000, of record).

It is noted that a type I diabetic human patient is not excluded from the scope of the instant invention as a 'human subject in need of treatment for obesity', but is expressly included. See Example 2. It is noted that a 70 kg patient is not excluded from the scope of the instant invention 'as a human subject in need thereof', but is expressly included. The human patient in need of the recited treatment according to the instant invention is expressly identified in the instant specification as one having a body weight of 70 kg. For example, the recited therapeutic amount range of 'about 0.1 milligrams per day to about 1 milligram per day', or 'about 0.01 to about 5 mg/day', or 0.03 to about 5 mg/day of the amylin agonist or amylin agonist analogue, pramlintide, administered is specifically "for a 70 kg patient". See lines 17-23 of page 27 of the instant specification; and lines 7-9 on page 13 of

Applicants' response filed December 2002. It is particularly noted that the mean body weight ± SEM of diabetic patients included in Kolterman's (1996) method who were administered subcutaneously with 30 micrograms, 100 micrograms, and 300 micrograms of pramlintide, three times a day for 14 days, was 70.6 ± 2.7, 74.4 ± 2.5, and 75.7 ± 2.6 respectively. Therefore, the 70.6 to 75.7 kg diabetic patients from Kolterman's (1996) study qualify as 'human subjects in need thereof' as recited in the instant claims.

It is noted that the claimed method of treating obesity in a human subject in need thereof encompasses alleviating the 'symptoms' of the disorder, i.e., obesity. See the last paragraph on page 9 of the substitute specification. The substitute specification at paragraph bridging pages 7 and 8 characterizes 'increased appetite' as a sign strongly associated with obesity (see second paragraph). Thus, increased appetite and therefore, increased food intake is viewed as a 'symptom' of obesity. It is further noted that the limitation 'treating obesity' is defined in the instant specification as including 'controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance', or preventing 'the onset of symptoms or complications, alleviating the symptoms or complications'. See second paragraph on page 9 of the substitute specification. A diabetic human patient having a baseline BMI of up to 27.0 kg/m^2 is not excluded from the scope of the instant invention 'as a human subject in need thereof', but is expressly included. See lines 26 and 27 of page 35 of the instant specification.

Kolterman et al. (1996) taught a method of subcutaneous administration of 30, 100, or 300 μg of pramlintide composition or AC137 (i.e., $^{25, 28, 29}$pro-h-amylin), a human amylin analogue peptide, to human patients with insulin-dependent diabetes mellitus or IDDM who are on insulin. Pramlintide was

administered three times daily for a period of 14 days. See abstract; and page 493. The mean body weight ± SEM of diabetic patients included in Kolterman's (1996) method who were administered subcutaneously with 30 micrograms, 100 micrograms, and 300 micrograms of pramlintide, three times a day for 14 days before meal, was 70.6 ± 2.7, 74.4 ± 2.5, and 75.7 ± 2.6 respectively. Therefore, the 70.6 to 75.7 kg diabetic patients from Kolterman's (1996) study qualify as 'human subjects in need of treatment of obesity' as recited in the instant claims. Additionally, even BMI-wise, Kolterman's (1996) diabetic subjects meet this limitation, because the diabetic subjects included in Kolterman's method (1996) had a BMI of up to 27 (see second full paragraph under 'Subjects, materials and methods). Therefore, Kolterman's (1996) diabetic subjects having a BMI at least in the range of 24 up to 27 do qualify as obese diabetic subjects in light of what was known in the art. For example, Itasaka et al. teach that a BMI of 24.0 to 26.4 represents mild obesity and 26.4 and heavier (i.e., including a BMI of 26.4 to 27) represents obesity in humans (see abstract of Itasaka et al). Kolterman's (1996) pramlintide composition did not comprise another obesity relief agent. The pramlintide composition was injected subcutaneously to the human patients (see 'Study design') and therefore is expected to inherently contain a pharmaceutically acceptable carrier therein. The amount administered was 30 micrograms three times a day to 'about 0.1 milligrams' or 300 micrograms per day. See 'Study design'; Table 1; and paragraph there below. Kolterman's (1996) subcutaneous administration of a therapeutically effective amount of the amylin agonist ^{25,28,29}Pro-human amylin to diabetic human subjects weighing 70 kg or more, or having a BMI falling in the BMI range of 24 up to 27 anticipates the instant claims. Thus, the very active step recited in the instantly claimed method was disclosed

and practiced by Kolterman et al. in April, 1996. Given that the method step in Kolterman's (1996) method and the instant claims are the same and the amount administered are the same, Kolterman's (1996) method is expected to necessarily bring about the same therapeutic effect in the pramlintide-treated diabetic patients as defined in the instant invention, i.e., by controlling body weight for cosmetic purposes, or by improving bodily appearance in the diabetic patients. Since the Office does not have the facilities for examining and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants to show a novel difference between the claimed method and the method of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594. Since the prior art clearly taught the claimed method, any assertions of specific functional properties attributed to the amylin agonist pramlintide peptide in the claimed method are merely inherent and do not necessarily make the claimed method patentable. The prior art method of administering the above-explained amount of the ^{25,28,29}Pro-human amylin (pramlintide or SEQ ID NO: 1) peptide to diabetic human subjects weighing 70 kg or more, and/or having a BMI falling in the range of 24 up to 27 necessarily serves as the Applicants' method of treating obesity as defined in the instant application, i.e., 'controlling weight for cosmetic purposes …, that is to control body weight to improve bodily appearance' in said diabetic human subjects.

Claims 76, 84 and 97 are anticipated by Kolterman et al. (1996).

20) Claims 76 and 84 are rejected under 35 U.S.C § 102(a) as being anticipated by Kolterman et al. (WO 96/40220, of record) ('220) as evidenced by Tsanev (Vutr. Boles 23: 12-17, 1984, abstract, of record).

It is noted that the inventorship of the Kolterman ('220) publication (Kolterman, Thompson, and Mullane) is non-identical with the inventorship of the instant application (Duft and Kolterman). Therefore, the publication of Kolterman et al. ('220) is proper prior art under 35 U.S.C. § 102(a). See MPEP 2132 III.

It is further noted that the limitation 'treating obesity' is defined in the instant specification as including 'controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance', or preventing 'the onset of symptoms or complications, alleviating the symptoms or complications'. See second paragraph on page 9 of the substitute specification. It is noted that the patient population used in the instant invention to treat obesity by the administration of the recited amount of pramlintide is insulin-requiring Type 2 diabetics. See Example 1 of the instant specification.

Kolterman et al. ('220) taught a method of administering to an insulin-taking type II diabetic human subject a dose of 10, 30, 50, 60 or 150 micrograms per day (i.e., the amount falling in the range recited in claim 82) of the amylin agonist analogue composition, pramlintide or $^{25, 28, 29}$pro-h-amylin, also known as AC137. The composition consists of pramlintide and a pharmaceutically acceptable carrier, and is administered in single or multiple doses, for example, in a dose of about 30 micrograms QID or about 60 micrograms TID or QID. See pages 9-11; paragraph bridging pages 20 and 21; page 21; first paragraph in page 19; lines 8-10 on page 19; and first row reciting 'Insulin-Treated Patients' in each Table. Pramlintide was administered subcutaneously 1-4 times a day before meals. See pages 9 and 22. Kolterman et al. ('220) additionally taught that the presence of obesity is a characteristic of 'most patients with Type II diabetes mellitus'. See page 10. Kolterman et al. ('220) taught the benefit of obtaining weight loss in Type II

diabetic patients by teaching that hyperglycemia associated with Type II diabetes can be reversed or ameliorated by weight loss sufficient to restore the sensitivity of the peripheral tissues to insulin (see pages 7, first paragraph), thus indicating that Type II diabetic patients are in need of weight loss. Thus, the very active step of the instantly claimed method was disclosed and practiced by Kolterman et al. ('220) in 1996 in the very same patient population used by Applicants in Example 1 of the instant application. The prior art method is the same as the instantly claimed method in terms of the peptide, pramlintide, administered, and the insulin-taking Type II diabetic patient population used, 80-90% of whom are known in the art to be intrinsically obese as taught by Tsanev (see Tsanev's abstract), the subcutaneous route of administration, the dose and the daily frequency of the amylin agonist administered, and the administration step prior to meals. Given Tsanev's express disclosure that 80 to 90% of type II diabetic patients are intrinsically obese, and given Kolterman's ('220) express teaching that obesity is a characteristic of 'most patients with Type II diabetes mellitus', Kolterman's ('220) method of subcutaneous administration of pramlintide to Type II diabetic patients in an amount that falls within the range recited in the instant claim necessarily serves as the claimed method of treating obesity and therefore anticipates the instantly claimed method. Kolterman's ('220) type II diabetic patients to whom pramlintide composition is administered necessarily qualify as human subjects in need of obesity as recited in the instant claims. Since the structural limitations of the instantly claimed method are clearly met by the teachings of Kolterman et al. ('220), Kolterman's ('220) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the same therapeutic effect. The Office's position that Kolterman's ('220) method is the same as the Applicants'

claimed method is based upon the fact that the method step, the compound administered, the amount of the compound administered, the route by which the compound is administered, and the intrinsically obese diabetic human patient population to which the compound is administered, are the same in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Kolterman's ('220) method of administration of the above-identified therapeutically effective amount of the amylin agonist [25,28,29]Pro-human amylin to intrinsically obese type 2 diabetic human subjects anticipates the instant claims. Given that the method step of the Kolterman's ('220) method and the instant claims are the same, Kolterman's ('220) method is expected to bring about a therapeutic effect against the intrinsic obesity in the pramlintide-treated type II diabetic patients as defined in the instant invention, i.e., by controlling body weight for cosmetic purposes, or by improving bodily appearance in the diabetic patients. Since the Office does not have the facilities for examining and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants to show a novel difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594. MPEP 2112 refers to In re Best to explain that something which is old does not become patentable upon the discovery of a new property; 'the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)'. Since the prior art clearly teaches the instantly claimed method, any assertions of specific functional properties attributed to the amylin

agonist peptide pramlintide in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 76 and 84 are anticipated by Kolterman et al. ('220). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Kolterman et al. ('220), but rather is used to show that every element of the claimed subject matter is disclosed by Kolterman et al. ('220), with the unrecited limitation(s) being inherent as evidenced by the state of the art. See In re Samour 197 USPQ 1 (CCPA 1978). Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of 80-90% of obesity in the diabetic subjects, is necessarily present in the thing described by Kolterman et al. ('220).

21) Claims 23, 33, 80 and 82 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Gaeta et al. (US 5,686,411, of record) ('411) as evidenced by Tsanev (Vutr. Boles 23: 12-17, 1984, abstract, of record).

The limitation 'is not administered in conjunction with another obesity relief agent' in claim 23 does not exclude the presence of an anti-diabetic agent, insulin, glucagon, a gastric emptying-inhibiting agent etc. in the recited composition.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 C.F.R 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention 'by another', or by an appropriate showing under 37 C.F.R 1.131.

Gaeta et al. (‘411) taught a method of administering to a mammal having diabetes mellitus, including a patient seen by a medical practitioner, i.e., a human, a therapeutically effective amount of the amylin agonist analogue of claim 6, i.e., amylin agonist analogue of SEQ ID NO: 14. See claims 31; and lines 45-53 in column 7 of the ‘411. Gaeta et al. (‘411) taught the ‘therapeutically effective amount’ of the amylin agonist to include the dosage units of 0.1 to 5 mg or 0.5 to 1.0 mg of the amylin agonist. See lines 53-59 in column 8. The amount effective to treat obesity, inhibit weight gain, or induce weight loss encompassed in the instant claims as described in the instant application, for example, about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls within the range of therapeutically effective amount of the amylin agonist disclosed in the ‘411 patent. Lines 9-14 of column 3 of the U.S. patent ‘411 describe that the limitation ‘diabetes mellitus’ includes insulin-requiring diabetes mellitus and that the administration was of amylin agonist analogue alone. The amylin agonist analogue composition comprises a pharmaceutical carrier and the amylin agonist analogue without insulin or glucagon. See lines 9-11 in column 7 and lines 37-39 in column 8. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev (see abstract), at least one of the diabetic patients administered with the amylin agonist analogue of SEQ ID NO: 14 in the method disclosed by the ‘411 patent qualifies as a human patient in need of treatment for obesity. Therefore, the method of the ‘411 patent comprising the administration of 0.1 to 5 mg, or 0.5 to 1.0 mg of the amylin agonist analogue of SEQ ID NO: 14 to a diabetic human anticipates the instant claims. Given that the method step of the ‘411 patent and the instant claims are the same, the amylin

agonist analogue of SEQ ID NO: 14, administered and the amount administered are the same, the method of the '411 patent is expected to bring about a therapeutic effect, weight gain-inhibiting effect, and weight loss-inducing effect in the intrinsically obese SEQ ID NO: 14 -treated insulin-requiring diabetic patient of Gaeta ('411) as defined in the instant invention. Since the structural limitations of the instantly claimed method and all of the criteria required by the instant claims are met by the teachings of the '411 patent, Gaeta's ('411) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain-inhibiting effect, or weight loss-inducing effect. The Office's position that Gaeta's ('411) method is the same as the Applicants' claimed method is based upon the fact that the method step, the amylin agonist analogue of SEQ ID NO: 14 administered, the amount of the SEQ ID NO: 14 administered, and the 80-90% intrinsically obese diabetic human patient to whom the SEQ ID NO: 14 was administered, are the same in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Gaeta's ('411) method of administration of the above-identified therapeutically effective amount (i.e., 0.1 to 5 mg, or 0.5 to 1.0 mg) of the amylin agonist analogue, SEQ ID NO: 14, to 80 to 90% of intrinsically obese type 2 diabetic human subject anticipates the instant claims. Given that the method step of the Gaeta's ('411) method and the instant claims are the same, Gaeta's ('411) method is expected to bring about the weight gain-inhibiting, weight loss-causing, or obesity-treating effect against the intrinsic obesity in the SEQ ID NO: 14-treated, insulin-requiring human diabetic patient. Since the Office does not have the facilities for examining and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants

to show a novel difference between the claimed method and the method of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594. MPEP 2112 refers to In re Best to explain that something which is old does not become patentable upon the discovery of a new property; 'the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)'. Since the prior art clearly teaches the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist analogue of SEQ ID NO: 14 in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 23, 33, 80 and 82 are clearly anticipated by Gaeta et al. ('411). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Gaeta et al. ('411), but rather is used to show that every element of the claimed subject matter is disclosed by Gaeta et al. ('411) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See In re Samour 197 USPQ 1 (CCPA 1978). 'To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' Continental Can Co. USA v. Monsanto Co., 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does

not preclude a finding of anticipation. Atlas Powder Co. v. IRECO Inc., 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in at least one of Gaeta's ('411) insulin-requiring diabetic subjects administered with SEQ ID NO: 14, is necessarily present in the thing described by Gaeta et al. ('411). The method of Gaeta et al. ('411) clearly anticipates the claimed method of the instant invention, because Gaeta et al. ('411) taught the very step of the instantly claimed method in the very same diabetic human patient. The alleged failure of Gaeta et al. ('411) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Gaeta et al. ('411). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See Mehl/Biophile International Corp. v. Milgraum, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing W.L. Gore & Assocs. v. Garlack, Inc., 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

22) Claims 76 and 84 are rejected under 35 U.S.C § 102(e)(2) as being anticipated by Gaeta et al. (US 5,686,411, of record) ('411) as evidenced by Tsanev (Vutr. Boles 23: 12-17, 1984, abstract, of record).

The limitation 'is not administered in conjunction with another obesity relief agent' in claim 76 does not exclude the presence of an anti-diabetic agent, insulin, glucagon, a gastric emptying-inhibiting agent etc. in the recited composition.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior

art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 C.F.R 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention 'by another', or by an appropriate showing under 37 C.F.R 1.131.

Gaeta et al. (‘411) taught a method of administering to a mammal having diabetes mellitus, including a patient seen by a medical practitioner, i.e., a human, a therapeutically effective amount of the amylin agonist of claim 19, ^{25,28,29}Pro-human amylin (SEQ ID NO: 12 or pramlintide). See claims 34, 35 and 19; and lines 45-53 in column 7 of the ‘411. Gaeta et al. (‘411) taught the ‘therapeutically effective amount’ of the amylin agonist to include the dosage units of 0.1 to 5 mg or 0.5 to 1.0 mg of the amylin agonist. See lines 53-59 in column 8. The amount effective to treat obesity, inhibit weight gain, or induce weight loss encompassed in the instant claims as described in the instant application, for example, about 0.01 milligrams to about 5 milligrams per day, about 0.05 milligrams to about 2 milligrams per day, or 300 micrograms per dose, falls within the range of therapeutically effective amount of the amylin agonist disclosed in the ‘411 patent. Lines 9-14 of column 3 of the U.S. patent ‘411 describe that the limitation ‘diabetes mellitus’ includes insulin-requiring diabetes mellitus and that the administration is of amylin agonist analogue alone. The amylin agonist composition comprises a pharmaceutical carrier and the amylin agonist without insulin or glucagon. See lines 9-11 in column 7 and lines 37-39 in column 8. Given the art-known prevalence of intrinsic obesity in 80% to 90% of diabetic patients as disclosed by Tsanev (see abstract), at least one of the diabetic patients administered with the amylin agonist ^{25,28,29}Pro-human amylin in the method

disclosed by the ‘411 patent qualifies as a human patient in need of treatment for obesity. Therefore, the method of the ‘411 patent comprising the administration of 0.1 to 5 mg, or 0.5 to 1.0 mg of the amylin agonist ^{25,28,29}Pro-human amylin to a diabetic human anticipates the instant claims. Given that the method step of the ‘411 patent and the instant claims are the same, the amylin agonist, ^{25,28,29}Pro-human amylin, administered and the amount administered are the same, the method of the ‘411 patent is expected to bring about a therapeutic effect, weight gain-inhibiting effect, and weight loss-inducing effect in the intrinsically obese ^{25,28,29}Pro-human amylin-treated insulin-requiring diabetic patient of Gaeta (‘411) as defined in the instant invention. Since the structural limitations of the instantly claimed method and all of the criteria required by the instant claims are met by the teachings of the ‘411 patent, Gaeta’s (‘411) method is expected to serve necessarily as the instantly claimed method and is expected to bring about the obesity-treating effect, weight gain-inhibiting effect, or weight loss-inducing effect. The Office’s position that Gaeta’s (‘411) method is the same as the Applicants’ claimed method is based upon the fact that the method step, the amylin agonist, ^{25,28,29}Pro-human amylin administered, the amount of the ^{25,28,29}Pro-human amylin administered, and the at least one intrinsically obese diabetic human patient to whom the ^{25,28,29}Pro-human amylin is administered, are the same in the two methods. The art-recognized intrinsic obesity being prevalent in 80 to 90% of diabetic patients as disclosed by Tsanev (see abstract), Gaeta’s (‘411) method of administration of the above-identified therapeutically effective amount (i.e., 0.1 to 5 mg, or 0.5 to 1.0 mg) of the amylin agonist ^{25,28,29}Pro-human amylin to at least one intrinsically obese type 2 diabetic human subject anticipates the instant claims. Given that the method step of the Gaeta’s (‘411) method and the instant claims are

the same, Gaeta's ('411) method is expected to bring about the weight gain-inhibiting, weight loss-causing, or obesity-treating effect against the intrinsic obesity in the [25,28,29]Pro-human amylin-treated, insulin-requiring human diabetic patient. Since the Office does not have the facilities for examining and comparing Applicants' claimed method with that of the prior art, the burden is on Applicants to show a novel difference between the claimed method and the method of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594. MPEP 2112 refers to In re Best to explain that something which is old does not become patentable upon the discovery of a new property; 'the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)'. Since the prior art clearly teaches the instantly claimed method, any assertions of specific functional properties attributed to the amylin agonist [25,28,29]Pro-human amylin in the claimed method are merely inherent and do not necessarily make the claimed method patentable.

Claims 76 and 84 are clearly anticipated by Gaeta et al. ('411). The publication of Tsanev is **not** used as a secondary reference in combination with the reference of Gaeta et al. ('411), but rather is used to show that every element of the claimed subject matter is disclosed by Gaeta et al. ('411) with the unrecited limitation(s) being inherent as evidenced by the state of the art. See In re Samour 197 USPQ 1 (CCPA 1978). 'To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the

reference, and that it would be so recognized by persons of ordinary skill.' Continental Can Co. USA v. Monsanto Co., 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. Atlas Powder Co. v. IRECO Inc., 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999). See MPEP 2124. Tsanev's extrinsic evidence makes clear that the missing descriptive matter, i.e., prevalence of obesity in at least one of Gaeta's ('411) insulin-requiring diabetic subjects administered with ^{25,28,29}Pro-human amylin, is necessarily present in the thing described by Gaeta et al. ('411). The method of Gaeta et al. ('411) clearly anticipates the claimed method of the instant invention, because Gaeta et al. ('411) taught the very step of the instantly claimed method in the very same diabetic human patient. The alleged failure of Gaeta et al. ('411) to expressly mention treatment of obesity as a goal is irrelevant. To the extent the method embodiment in the claimed invention achieves treatment of obesity, so does the method of Gaeta et al. ('411). Where the result is a necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results. See Mehl/Biophile International Corp. v. Milgraum, U.S. Court of Appeals Federal Court, 52 USPQ2d 1303 and 1306, 192 F3d 1362, 1999 citing W.L. Gore & Assocs. v. Garlack, Inc., 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983).

Relevant Prior Art

23) The art made of record and not currently relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

Olefsky JM (In: *Harrison's Principles of Internal Medicine*, 12th Edition, McGraw-Hill Book Company, pages 411-416, 1961, of record) documented in 1961 that the type of diabetes wherein 80 to 90% are 'obese' is type II diabetes. See the first full paragraph on page 414.

Remarks

24) Claims 23, 27, 29, 31-33, 37-39, 76, 80, 82, 84 and 95-97 stand rejected.

25) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

26) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

27) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to

4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's acting supervisor, Gary Nickol, can be reached on (571) 272-0835.

/S. Devi/
Primary Examiner
AU 1645

March, 2011